IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: Lobb et al.	Art Unit	: 1644
Serial No.	: 09/251,073	Examiner	: P. Gambel
Filed	: February 16, 1999		
Title	: TREATMENT FOR ASTHMA		

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

BRIEF ON APPEAL

(1) Real Party in Interest

The Real Party in Interest is Biogen Idec, Inc., 14 Cambridge Center, Cambridge, MA 02142.

(2) Related Appeals and Interferences

There are no pending related appeals or interferences.

(3) Status of Claims

Claims 1-3, 6, 7, 9-13, 17, 18, 26-37 are rejected.

Claims 4, 5, 8, 14-16, and 19-25 have been canceled.

(4) Status of Amendments

No amendments are being submitted herewith.

CERTIFICATE OF MAILING BY FIRST CLASS MAIL

I hereby certify under 37 CFR §1.8(a) that this correspondence is being deposited with the United States Postal Service as first class mail with sufficient postage on the date indicated below and is addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

3-22-04
Date of Deposit

Bethany Slack
Signature

BETHANY SLACK
Typed or Printed Name of Person Signing Certificate

(5) Summary of Invention

The invention relates to methods of treatment of allergic asthma. In some instances, for example those methods corresponding to claim 1 and those claims depending therefrom, the methods include identifying a mammal suffering from allergic asthma and administering to the mammal a composition including a soluble fibronectin polypeptide. In other instances, for example those methods corresponding to claim 12 and those claims depending therefrom, the methods include identifying a mammal suffering from allergic asthma and administering to the mammal a soluble fibronectin polypeptide capable of binding to the α4 subunit of VLA-4 in an amount effective to provide inhibition of late phase response to an allergen to which the sufferer is hyersensitive, or to provide decreased airway hypersensitivity in said mammal following allergen challenge.

(6) Issues

Are claims 1-3, 6, 7, 9-13, 17, 18, 26-37 obvious over U.S. Patent No. 5,730,978 to Wayner et al. ("Wayner") and/or U.S. Patent No. 5,510,332 to Kogan et al. ("Kogan"), and/or U.S. Patent No. 6,117,840 to Arrhenius et al. ("Arrhenius")?

(7) Grouping of Claims

Claims 1-3, 7, 9-13, 17, 18, and 26-37 stand or fall together.

(8) Argument

Claims 1-3, 7, 9-13, 17, 18, and 26-37 are rejected under U.S.C. § 103(a) as being unpatentable over Wayner and/or Kogan and/or Arrhenius in view of art known of the nature and treatment of asthma at the time the invention was made. This rejection is respectfully traversed.

To establish prima facie obviousness of a claimed invention, the prior art reference (or references when combined) must teach or suggest all the claim limitations. In addition, there must be a motivation to combine or modify the reference(s) to arrive at the claimed invention, and a reasonable expectation of success. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and

not based on Applicants' disclosure. (See M.P.E.P. § 2142, citing In re Vaeck, 947 F.3d 488 (Fed. Cir. 1991).) Here a *prima facie* case of obviousness has not been made because nothing in the prior art of record would have led the artisan to pick and choose the specific aspects from the references and modify them to administer a soluble fibronectin polypeptide to a patient suffering from allergic asthma with a reasonable expectation of success.

Both Wayner and Kogan broadly disclose diseases that might be treated by inhibiting α4β1 integrin binding. Some of the diseases described in Wayner include those diseases associated with chronic or relapsing activation of the immune system, including collagen vascular diseases and other autoimmune diseases including systemic lupus erythematosis and rheumatoid arthritis, multiple sclerosis, asthma, and allergy, "to name but a few". (See Wayner Col. 16, lines 17-26.) Wayner further asserts that the disclosed methods can be used to treat relatively acute activations of the immune system including graft versus hose disease, allograft rejection or transfusion reaction. (See Wayner Col. 16, lines 15-30.) Some examples of the diseases described in Kogan include atherosclerosis, rheumatoid arthritis, asthma, allergy, multiple sclerosis, and type I diabetes. (See Kogan Col. 2, lines 3-7.)

Neither Wayner nor Kogan provide any *in vivo* data or animal models to support a conclusion that administration the claimed compound, i.e., a soluble fibronectin polypeptide, would effectively treat asthma, much less allergic asthma as required by the claims. Instead, the only data provided by Wayner and Kogan is from *in vitro* experiments. While *in vitro* data can serve to characterize a biochemical pathway, one of skill in the art would look only to *in vivo* data to identify the crucial roles of adhesion molecules in a human pathology. Thus, while Wayner and Kogan disclose a wide variety of potential diseases ranging from diabetes, to asthma to multiple sclerosis that could be treated by inhibiting α4β1 binding, nothing in Wayner and/or Kogan provides motivation to one of skill in the art to specifically administer a soluble fibronectin polypeptide for the treatment of allergic asthma.

Applicants' disagree with Examiner's conclusory assertion that "from the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention." (See Office Action, page 6, first paragraph.) Rather, one of skill in the art would not reasonably expect that a single compound,

e.g., a soluble fibronectin polypeptide, would be successful in the treatment of all of the diseases, or even most of the diseases, disclosed in Wayner and Kogan. Moreover, nothing in Wayner or Kogan provides a reasonable expectation that asthma, in particular allergic asthma, would be effectively treated with the disclosed compounds, in particular fibronectin. Instead, both Wayner and Kogan provide only *in vitro* data, which simply characterizes the disclosed biochemical pathway. Without more, it cannot be fairly said that one of skill in the art would reasonably expect that treatment of allergic asthma with a soluble fibronectin polypeptide would be successful.

Arrhenius fails to make up for the deficient teachings of Wayner and Kogan. While Arrhenius discloses *in vivo* data demonstrating a treatment of asthma, Arrhenius does not use soluble fibronectin polypeptides as required by the claims, but instead uses highly modified peptidomimetic agents with amide ring-containing groups at both the N- and C- terminus (see columns 8-9 and Table 1 of Arrhenius). In fact, Arrhenius teaches away from fibronectin polypeptides, such as CS-1 peptides, by describing their drawbacks and stating, for example at Col. 4, lines 54-56 (the background section), that the CS-1 peptide "is large and costly to make, and also is subject to rapid degradation."

The Examiner cites In re Farrenkopf, 713 F.2d 714 (Fed. Cir. 1983) for the assertion that economic reasons alone are not sufficient to dissuade a person of skill in the art from making a proposed modification or combination. (See Office Action, page 5, third full paragraph.) However, the Examiner's reliance upon In re Farrenkopf is misplaced, as Arrhenius provides technical reasons, not merely economic reasons, that teach away from modifying the compound of Arrhenius to make Applicants' featured fibronectin polypeptide, namely Arrhenius discloses that the Applicant's polypeptide is purportedly "subject to rapid degradation." At the very least, this statement clearly supports the notion that there was no reasonable expectation of success to arrive at the claimed methods. Even more, a skilled artisan reading Arrhenius would have been led away from the present invention. Because Arrhenius, either alone or in combination with Wayner and/or Kogan, fails provides a motivation and reasonable expectation of success to administer a soluble fibronectin polypeptide for the treatment of allergic asthma, a *prima face*

case of obviousness has not been made, and Applicants respectfully request that the rejection be withdrawn.

In view of the foregoing, Applicants assert that the pending claims are in condition for allowance, of which action is requested.

The brief fee of $330 is enclosed. Please apply any other charges or credits to Deposit Account No. 06-1050, referencing attorney docket number 10274-003003.

Respectfully submitted,

Date: 22 March 2004

for: Louis Myers, Reg. No. 50,635
Louis Myers
Reg. No. 35,965

Fish & Richardson P.C.
225 Franklin Street
Boston, MA 02110-2804
Telephone: (617) 542-5070
Facsimile: (617) 542-8906

20806658.doc

Appendix of Claims

1. A method for the treatment of allergic asthma comprising:

identifying a mammal suffering from allergic asthma; and

administering to the mammal a composition comprising a soluble fibronectin polypeptide.

2. The method of Claim 1, wherein the composition is administered intravenously.

3. The method of Claim 1, wherein the composition is administered in the form of an aerosol by inhalation.

6. The method of Claim 1, wherein the composition is administered at a dosage so as to provide from 0.05 to 5.0 mg/kg of fibronectin polypeptide, based on the weight of the asthma sufferer.

7. The method of Claim 6, wherein the composition is administered to the mammal at a dosage so as to provide 0.5 to 2.0 mg/kg of fibronectin polypeptide, based on the weight of the asthma sufferer.

9. The method of Claim 1, wherein the composition is administered prior to exposure to an allergen to which the asthma sufferer is hypersensitive.

11. The method of Claim 1, wherein the composition is administered to the mammal after exposure to an allergen to which said mammal is hypersensitive.

12. A method for the treatment of allergic asthma comprising:

identifying a mammal suffering from allergic asthma; and

administering to the mammal a soluble fibronectin polypeptide capable of binding to the α4 subunit of VLA-4, in an amount effective to provide inhibition of late phase response to an allergen to which the sufferer is hypersensitive or to provide decreased airway hypersensitivity in said mammal following allergen challenge.

13. The method of Claim 12, wherein the soluble fibronectin polypeptide comprises an EILDV motif (SEQ ID NO.: 16).

17. The method of Claim 12, wherein the composition is administered at a dosage so as to provide from 0.05 to 5.0 mg/kg of polypeptide, based on the weight of the asthma sufferer.

18. The method of Claim 17, wherein the composition is administered at a dosage so as to provide 1.0-2.0 mg/kg of polypeptide, based on the weight of the asthma sufferer.

26. The method according to Claim 1, wherein the soluble fibronectin polypeptide comprises an EILDV motif (SEQ ID NO.: 16).

27. The method according to Claim 1, wherein the soluble fibronectin polypeptide comprises an alternatively spliced non-type III connecting segment.

28. The method of Claim 12, wherein the soluble fibronectin polypeptide comprises an alternatively spliced non-type III connecting segment.

29. The method of Claim 12, wherein the mammal is a human.

30. The method of Claim 1, wherein the composition is administered to the mammal at the time or immediately after allergen exposure.

31. The method of Claim 1, wherein the composition is administered to the mammal between the early phase and late phase response.

32. The method of Claim 12, wherein the composition is administered to the mammal prior to exposure to an allergen to which the asthma sufferer is hypersensitive.

33. The method of Claim 12, wherein the composition is administered to the mammal at the time or immediately after allergen exposure.

34. The method of Claim 12, wherein the composition is administered to the mammal between the early phase and late phase response.

35. The method of Claim 12, wherein the composition is administered to the mammal after allergen exposure.

36. The method of Claim 12, wherein the composition is administered intravenously.

37. The method of Claim 12, wherein the composition is administered in the form of an aerosol by inhalation.